

Clinical respiratory infections and pneumonia during the Hajj pilgrimage: A systematic review

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Abstract

BACKGROUND: The Islamic Hajj pilgrimage to Mecca is one of the world's largest annual mass gatherings. Inevitable overcrowding during the pilgrims' stay greatly increases the risk of acquiring and spreading infectious diseases, especially respiratory diseases.

METHOD: The MEDLINE/PubMed and Scopus databases were searched for all relevant papers published prior to February 2018 that evaluated the prevalence of clinical symptoms of respiratory infections, including pneumonia, among Hajj pilgrims, as well as their influenza and pneumococcal vaccination status.

RESULTS: A total of 61 papers were included in the review. Both cohort- and hospital-based studies provide complementary data, and both are therefore necessary to provide a complete picture of the total burden of respiratory diseases during the Hajj. Respiratory symptoms have been common among Hajj pilgrims over the last 15 years. In cohorts of pilgrims, cough ranged from 1.9% to 91.5%. However, the prevalence rates of the most common symptoms (cough, sore throat, and subjective fever) of influenza-like illness (ILI) varied widely across the included studies. These studies have shown variable results, with overall rates of ILI ranging from 8% to 78.2%. These differences might result from differences in study design, study period, and rates of vaccination against seasonal influenza that ranged from 1.1% to 100% among study participants. Moreover, the definition of ILI was inconsistent across studies. In hospitalized Hajj pilgrims, the prevalence of pneumonia, that remains a major concern in critically ill patients, ranged from 0.2% to 54.8%.

CONCLUSIONS: Large multinational follow-up studies are recommended for clinic-based syndromic surveillance, in conjunction with microbiological surveillance. Matched cohorts ensure better comparability across studies. However, study design and data collection procedures should be standardized to facilitate reporting and to achieve comparability between studies. Furthermore, the definition of ILI, and of most common symptoms used to

52 define respiratory infections (e.g., upper respiratory tract infection), need to be precisely
53 defined and consistently used. Future studies need to address potential effect of influenza and
54 pneumococcal vaccine in the context of the Hajj pilgrimage.
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Introduction

The yearly "*Hajj*" (also known as the pilgrimage to Mecca) in the Kingdom of Saudi Arabia (KSA) is the "Fifth Pillar of Islam" and is mandatory once in a lifetime for all adult Muslim who are physically and financially able. The Hajj is one of the world's largest annual mass gatherings. In 2016, around 1.3 million foreign visitors, from more than 180 countries, gathered in the KSA to complete the Hajj, in addition to over 500,000 domestic Hajj pilgrims [1]. Also, about 5-6 million pilgrims perform the "*Umrah*" (also known as the lesser pilgrimage) each year.

The Hajj and its rituals are physically demanding for Hajj pilgrims, the majority of whom are elderly [2], with chronic conditions. Although the Hajj rituals only take one week, pilgrims usually stay in the KSA for several weeks throughout the month-long Hajj season, presenting a major public health and infection control concern, and a challenge both for the Saudi authorities, as well as for the national authorities of the countries of origin of the pilgrims. In addition to physical exhaustion, sleep deprivation [3], and heat stress [4], inevitable overcrowding, both in housing and ritual sites, especially in Mina encampment (this is approximately a 3-kilometer square area where pilgrims are accommodated in air-conditioned semi-permanent tents, some with up to 50-100 people) and inside the Sacred Mosque in Mecca (with up to six pilgrims per square meter) [5], greatly increases the risk of acquiring and spreading infectious diseases [6-8], especially respiratory diseases [9,10]. To minimize the spread of infections during the pilgrimage or in the pilgrims' home countries upon their return, vaccination and non-pharmaceutical interventions are thus recommended by national and international public health agencies [11,12].

We carried out a systematic review of cohort and hospital studies that reported the prevalence of clinical symptoms of respiratory infections and pneumonia among pilgrims during the Hajj, and both their influenza and pneumococcal vaccination status, with the aim to provide data

allowing the investigation of the impact of this large mass-gathering event on public health policies and services and to identify potential targets for preventive measures.

Search Strategy and Selection Criteria

This review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (<http://www.prismastatement.org>).

The MEDLINE/PubMed and Scopus databases were searched for all relevant papers published prior to February 2018, using the terms:

#1: Hajj OR hadj OR pilgrim OR pilgrims OR pilgrimage

#2: Respiratory

#3: Infection OR infections

#4: ILI OR URTI OR URTIs OR URI OR URIs OR LRTI OR LRTIs OR LRI OR LRIs

#5: Pneumonia OR *Streptococcus pneumoniae* OR pneumococcus OR pneumococcal

#6: #1 AND ((#2 AND #3) OR (#4) OR (#5))

In addition, the Saudi epidemiology bulletin (<http://seb.drupalgardens.com/>) was hand searched for additional papers for inclusion. Finally, the reference lists of reviewed articles were searched for additional relevant papers.

For inclusion, the article had to meet the following criteria: (1) Original study involving Hajj pilgrims; (2) detailed description of the study population, including influenza and pneumococcal vaccination status when available; (3) clinical or self-reported respiratory symptoms and diseases. Only articles published in English were included for review. We excluded cohort studies with less than 50 participants and case reports. We also excluded studies conducted among selected groups of individuals suffering from respiratory tract infections, due to lacking denominator data.

The two authors independently performed the searches, screened titles/abstracts for eligibility, selected papers that appeared to be relevant according to the review's inclusion criteria, and

reviewed each of the selected manuscripts in full. The data were extracted from the included papers by one reviewer (SB) and collected in the summary table that was included in the review. The extracted data were checked by the two authors (SB and PG) for accuracy. Minor discrepancies were resolved by the authors' discussion.

Results

Included studies

The search strategy initially yielded 391 records, of which 143 were duplicates. Twenty-nine additional papers were identified through manual searches. Of the 277 papers identified 183 records were excluded after screening the title and abstract. Of the 94 full text articles reviewed, 61 were deemed suitable for inclusion in this review according to the inclusion/exclusion criteria. The results of the search strategy are shown in Figure 1.

Cohort studies addressing the prevalence of respiratory tract infections among Hajj pilgrims

A total of 45 publications were identified. These studies were conducted among cohorts of pilgrims from the 1999 through the 2015 Hajj seasons. The results of these studies are presented in Table 1. Various study designs were used, including cross-sectional studies, case-control studies, and prospective cohort studies with follow-up of pilgrims, before, during and after the Hajj. Participants were from different countries and continents (Africa, North America, Asia, Europe, as well as from Australia), with the majority from Iran, and they were recruited from different settings, including travel medicine clinics, vaccination centers, Hajj travel agencies, international airports and transit zones, Mecca's city and Mina encampments. Their numbers varied widely in these studies, ranging from 106 to 107,074. Respiratory symptoms were common during the Hajj. Overall, the prevalence of cough ranged from 1.9% in domestic and international pilgrims in 1999 [13] to 91.5% in Malaysian pilgrims in 2007 [14,15] (Table 3). More recent studies, conducted in different populations of

pilgrims during the 2011-2014 Hajj seasons, reported prevalence of cough ranging from 46.3% to 86.8% [16-24]. These studies also reported a comparable prevalence of sore throat ranging from 34.7% to 91% among pilgrims [16-23].

In addition, many of these studies have investigated the epidemiology of respiratory tract infections among pilgrims by estimating the common prevalence of upper respiratory tract infection (URTI), acute respiratory infection (ARI) or influenza-like illness (ILI), which were inconsistently defined across studies by a combination of general symptoms (e.g. cough, sore throat and fever). Overall prevalence of ILI varied in these studies from 8% to 78.2% [14-16,18-23,25-45] (Table 3). In large studies conducted among Iranian pilgrims between 2003 and 2005, the prevalence of ILI was, respectively, 70.1% and 35.8% in 2003 and 2004 [41,42], but 19.6% in 2005 [46]. In another large 5-year (2004-2008) follow-up study conducted among 254823 Iranian pilgrims, only 10.7% of pilgrims complained of ILI during the Hajj [47,48]. However, the ILI syndromic case definition used in the 2003-2004 study (ILI was defined as cough and fever of more than 38°C with or without the coryzal symptoms and myalgia) [41,42] was different with that used in the 2004-2008 study (ILI was defined as symptoms and signs such as sudden headache, dry cough, high grade fever, myalgia, coryza, malaise and loss of appetite with an abnormal general appearance) [47,48]. Also, it is unclear from the 2005 study [46] if the definition used was consistent with those used in the two previous studies [41,42,47,48]. In a recent large study, conducted among 3364 Egyptian pilgrims between 2012 and 2015, the prevalence of ILI was 30.4% (ILI was defined according to the World Health Organization definition as the presence of measured fever of $\geq 38^{\circ}\text{C}$, and cough; with onset within the last 10 days) [45]. Other studies of different sizes (from 129 to 468) and design were conducted from 2007 through 2014 among different populations of pilgrims using a common ILI definition (the association of cough, sore throat, and subjective fever). These studies have shown variable results, with overall rates of ILI ranging from 8% to

78.2% [14-16,18,19,21-23,25-26,31,35,37]. Thus, during the 2013 Hajj season, while the highest prevalence of ILI was observed among Malaysian pilgrims, with a prevalence estimated at 78.2% [25], a lower prevalence was observed among French pilgrims (47.3%) [18,21].

Coverage of seasonal influenza vaccination among pilgrims was evaluated in many studies, which have yielded varying results, with reported rates of influenza vaccination ranged from 1.1% to 100% [14,15,18,21-23,25,26,28,29,31-34,36,37,41-51,53-56]. A variation over time in influenza vaccination coverage was observed, as exemplified by a rate of 10.5% observed in a survey of pilgrims from Riyadh in 2003 [43], but 94.4% in a similar survey in 2010 [32,33,36]. During the 2013 Hajj season, influenza vaccination rates also varied according to pilgrims' country of origin [29], with 20% observed among Saudi pilgrims, 80% among Qatari pilgrims, and 87% among Australian pilgrims, while a study involving French pilgrims interestingly reported that none of them had received the 2013 influenza vaccine before departing for the Hajj because the vaccine was not available at this time [18,21]. The majority of the studies reported influenza vaccination coverage among pilgrims, but only 13 [18,19,21-23,25,27,28,31,46-48,55] reported their pneumococcal vaccination status, with rates ranging from 1.2% among a multinational cohort of 1676 pilgrims from 13 countries (from Africa, Asia, USA and Europe) in 2013 [28] to 51.2% among a small study of 129 French pilgrims in 2013 [18,21].

Hospital-based studies addressing the prevalence of respiratory tract infections among ill Hajj pilgrims

Of the 61 publications that were included in this review, 16 specifically addressed ill Hajj pilgrims at health care facilities from 1993 through 2014 Hajj seasons. Medical facilities included primary health care centers (PHCCs) and different specialized wards in tertiary care hospitals, including ear, nose and throat (ENT) departments, intensive care units, emergency

units, infectious disease units and unspecified medical units. Pilgrim participants were included either as inpatients or outpatients. The results of these studies are summarized in Table 2.

Overall, the prevalence of upper respiratory tract infections (URTI) ranged from 1.4% to 42.1% (Table 3). This prevalence was 1.4% among 141 Pakistani pilgrims who attended the King Abdul Aziz hospital in Medina during the 1992 Hajj [57] and 42.1% among 3087 Saudi and non-Saudi patients (47.5% of them were pilgrims) who attended the ENT clinic at Al-Noor Specialist Hospital in Mecca during the 2009 Hajj [58]. Pharyngitis was also frequently reported among ill pilgrims. Thus, in this study of 3087 pilgrims during the 2009 Hajj, the overall prevalence of pharyngitis was 45.7% [58]. More recently, in 2008, the prevalence of pharyngitis in a large cohort of 4136 outpatients patients from 82 nationalities who attended 13 randomly selected Mina PHCCs (94.9% of whom were pilgrims) was found to be 23.7% [59,60], and 61% in a study of 1047 Saudi and non-Saudi patients (2.3% of them were inpatients) [61]. However, in this second study of 1047 patients, only 34.5% were pilgrims.

On the contrary, lower prevalence rates of bronchitis were reported during the Hajj (1.4%-9.6%) [59-63]. A recent retrospective cross-sectional multicenter study of 185 Turkish inpatients (87.5% were pilgrims) who returned to Turkey from the Arabian Peninsula countries between 2012 and 2014 reported a slightly higher prevalence of acute tracheobronchitis (13.6%) [64]. In addition, in this study, pneumonia was among the most common clinical diagnosis among the hospitalized Hajj patients and represented about half of diagnoses [64]. As pneumonia remains a major concern in critically ill patients, most of them reported the prevalence of pneumonia among pilgrims [57,59,60,62-71], with reported rates ranging from 0.2% in 2008 in 13 randomly selected Mina primary health care centers [59,60] to 54.8% in 2004 in two ICU in Mecca [68] (Table 3). The prevalence of pneumonia was not reported in 3 papers [58,61,72]. Pneumonia was the second most common admitting diagnosis

(22%) in a study of 140 patients admitted to the ICUs in four hospitals in Mina during the 2004 Hajj [68]. This result is further confirmed by a recent study of 452 critically ill Hajj patients, of over 40 nationalities, admitted to 15 hospitals in 2009 and 2010. In this study, pneumonia was defined as the primary cause of critical illness (27.2%) of all ICUs admissions during the Hajj [65]. Also, in another prospective study of pilgrims admitted in two major ICUs in Mecca for the 2004 Hajj season, community acquired pneumonia (CAP) was the commonest source of sepsis, 54.8% [66].

Discussion

The purpose of this review was to provide syndromic surveillance data that may be useful, in conjunction with microbiological data that will be presented in further papers, for the surveillance of respiratory infections and pneumonia during the Hajj. Despite the fact that some of the included studies in our review were performed among small numbers of pilgrims and cannot be extrapolated, it is clear from this work that respiratory symptoms have been common among Hajj pilgrims over the last 15 years, as evidenced by the high prevalence of cough (over 90%) among Malaysian pilgrims during the 2007 Hajj [73]. Cough is a common symptom among pilgrims [16,74] and likely results from crowded conditions during the Hajj. This close contact among such individuals may increase the risk of the transmission of respiratory pathogens, and therefore may contribute to respiratory disease outbreaks. Climatic conditions and air pollution in Mecca and surrounding holy sites during the Hajj [75] may also play a role. Recent follow-up studies thus evidenced a significant acquisition of respiratory viruses, particularly rhinovirus, influenza virus, and coronaviruses other than Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and of bacteria, including *Streptococcus pneumonia*, *Hemophilus influenza*, *Staphylococcus aureus* and *Klesiella pneumonia* by Hajj pilgrims upon their return from the Hajj [76,77]. Respiratory diseases are the most common diseases observed among pilgrims attending Mina primary health care

centers [59] and a major cause of hospital admission during the Hajj [70], with pneumonia a leading cause of admission to intensive care units [62,68], where they are responsible for about half of the cases of sepsis [66]. Unfortunately, while numerous articles on Hajj pilgrims were retrieved from our literature search, relatively few recent articles specifically addressed ill pilgrims in the context of hospital settings. The use of cohort studies allows investigators to evaluate the actual incidence of clinical events in Hajj pilgrims since it provides a denominator, but may not identify and capture the prevalence of some underlying conditions and of severe forms of respiratory tract infections, which are more likely to be evidenced in hospital patient populations. Conversely, hospital studies use data that may be biased, frequently lacking denominator values, and so probably overestimating the occurrence of severe illness. Moreover, a hospital-based study will, by definition, not capture some minor illness cases that do not require hospitalization.

The prevalence rates of cough, sore throat and subjective fever varied widely across the included studies. These differences may result from differences in study design that may lead to potential biases (for example bias related to the method of data collection, using either self-report questionnaires or telephone interview), study period (with regards to the seasonality of respiratory viral infections), and rates of vaccination against seasonal influenza among study participants which may widely vary from one study to another, as described in this review. Thus, all data regarding the pilgrims, including demographic data, medical history, clinical data and information on vaccination status and compliance with non-pharmaceutical preventive measures, should be carefully collected by using standardized questionnaires. In addition, in the context of syndromic surveillance for respiratory pathogens, data regarding the pilgrim's symptoms should be collected prospectively during face-to-face interviews by trained medical investigators who travel with the pilgrims. One important result of this review is the finding of a lack of consistency ILI syndromic case definitions across included studies.

Thus, in a 2003 study (that did not fulfill the inclusion criteria for this review) [78], of 1310 Malaysian pilgrims who had a clinic visit for upper respiratory tract symptoms at five clinics during the 2000 Hajj, with the aim of determining influenza vaccine effectiveness against clinically defined ILI, 63% had ILI (defined as sore throat in combination with either temperature $\geq 38^{\circ}\text{C}$ or cough) and 14% had influenza by the CDC definition (defined as measured fever [$\geq 100^{\circ}\text{F}$ (37.8°C)] and a cough and/or a sore throat). Only one of the studies reported here used the CDC definition of ILI or the WHO definition (an acute respiratory infection with measured fever of $\geq 38^{\circ}\text{C}$ and cough, with onset within the last 10 days) [45].

In his paper, Rashid et al. demonstrated the low sensitivity of the CDC criteria and proposed therefore the use of the triad of ‘cough, sore throat and subjective fever’ to clinically define ILI at the Hajj or other mass gatherings, since this new simple clinical case definition is more specific and sensitive than the CDC definition [79]. This definition was used over the last years by French [16,18,19,21-23,31,37], Malaysian [14,15,25], Indian [26] and Afghan [35] investigators leading cohort studies among Hajj pilgrims, thus allowing more reliable comparisons of findings between studies (Table 1).

Respiratory diseases are a major concern during the Hajj. Non-pharmaceutical interventions (e.g., hand hygiene, wearing face masks, social distancing) are known to reduce the spread of respiratory viruses from person to person and are therefore recommended to pilgrims by public health agencies. Although hand hygiene compliance is high among pilgrims, face mask use and social distancing remain difficult challenges. Data about the effectiveness of these measures for preventing acute respiratory infections at the Hajj are limited, and results are contradictory, highlighting the need for future large-scale studies [80].

In addition to non-pharmaceutical interventions, vaccination against influenza is recommended for all Hajj pilgrims by the Ministry of Health of Saudi Arabia [11,12].

Differences in study design and heterogeneity in the ILI definition across studies make it

difficult to compare findings from different studies and inhibits the drawing of conclusions regarding the potential effects of this vaccination on related clinical symptoms of influenza disease. However, recent papers by Alqahtani et al. and Alfelali et al. found the influenza vaccine to be effective, respectively, against both laboratory-confirmed influenza [81] and clinical influenza [82]. As influenza vaccination is generally considered effective in reducing influenza-related infections, the Scientific Committee for Influenza and Pneumococcal Vaccination guidelines (SCIPV) thus recommends, in its recent guidelines, an influenza vaccination for all people, especially those at high risk, at least 2 weeks before the Hajj [83]. It also recommends, for the next Hajj seasons that will take place from June to September, the administration (prior to the Hajj) of the Southern Hemisphere influenza vaccine for pilgrims from the Southern Hemisphere (where influenza positivity rates are higher during this period). Furthermore, as the influenza vaccine is not expected to be available for pilgrims from the Northern Hemisphere before these next Hajj seasons, the SCIPV also recommends the administration of the Southern Hemisphere influenza vaccine for those pilgrims from the opposite hemisphere before the Hajj [83]. Because of the mismatching between circulating and vaccine strains that has frequently occurred since 2003 [84], Alfelali et al. recommends, when the composition of influenza vaccines differs and whenever logistically feasible, taking into consideration the dual vaccination of Hajj pilgrims with both the Southern and Northern Hemispheres' vaccines. However, such strategy is impaired by the frequent unavailability of the Southern Hemisphere influenza vaccine in the Northern Hemisphere. The issue of influenza vaccine availability to match Southern and Northern hemispheres was discussed by the Saudi Ministry of Health in consultation with the WHO and it was recommended to use the available hemisphere strain as long as there is a match in circulating strains [85]. Despite the risk of acquisition of *S. pneumoniae* during the Hajj, there is currently no consistent guideline on the use of pneumococcal vaccine for Hajj pilgrims across pilgrim countries of

origin [86,87]. Thus, and because many of the Hajj pilgrims are elderly and have chronic illnesses and underlying risk conditions for which pneumococcal vaccination is recommended [86], the SCIPV also recommended, in its 2016 pneumococcal vaccination guidelines, pneumococcal vaccination of the at-risk population at the appropriate time before the Hajj, using the 2 types of pneumococcal vaccines that are currently available: the 23-valent polysaccharide pneumococcal vaccine (PPSV23) and the 13-valent conjugate vaccine (PCV13) [88]. However, it did not recommend providing a pneumococcal vaccine routinely to healthy persons aged less than 50 years, because of lack of evidence. In addition, it has been well demonstrated that the conjugate vaccine against *S. pneumoniae* targets the most virulent serotypes associated with Invasive Pneumococcal Diseases (IPD) that are also associated with antibiotic resistance [89]. These arguments reinforce the need for compliance with current recommendations for vaccinating at-risk Hajj pilgrims against IPD and influenza [89].

Respiratory tract infections, including influenza, continue to be a major concern during the Hajj. Both cohort- and hospital-based studies provide complementary data and potentially useful information, and both are therefore necessary to provide a complete picture of the total burden of respiratory diseases during this mass gathering. Large multinational follow-up studies are thus recommended for clinic-based syndromic surveillance, in conjunction with microbiological surveillance. Matched cohorts ensure better comparability across studies, particularly in terms of origin of pilgrims and possible travelling conditions. However, the study design and data collection procedures should be standardized, to facilitate reporting and to achieve comparability between studies. Furthermore, the definition of ILI, and of most common symptoms used to define respiratory infections (e.g., URTI), needs to be precisely defined and consistently used. Future studies need to address the potential effects of influenza and pneumococcal vaccine in the context of the Hajj pilgrimage. Moreover, because of the

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364 The authors have no conflicts of interest to declare.

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Table 1. Studies conducted among cohorts of Hajj pilgrims

Hajj season	Study population	Study design	Global prevalence of respiratory symptoms (%)	Vaccination coverage (%)	Study	Ref.
2013-2015	847 Chinese pilgrims	Longitudinal survey conducted in returning Hajj pilgrims arriving at Xinjiang and Gansu airports, China	Fever: 1.9% Sore throat or cough: 1.9%	Influenza: 100%	Ma <i>et al.</i> , 2017 (BMC Infectious Diseases)	[50]
2014	148 Iranian pilgrims	Follow-up seroepidemiological study among Hajj pilgrims returning to Yazd province, Iran	Cough: 63%	Not specified	Rahimian <i>et al.</i> , 2017 (Respiratory Medicine)	[24]
2012-2015	3364 Egyptian pilgrims	A cross-sectional survey among Hajj pilgrims at Cairo Airport, Egypt. Study based on face-to-face interview	ILI ¹ : 30.4%	Influenza: 19.7%	Refaey <i>et al.</i> , 2017 (Influenza Other Respi Viruses)	[45]
2013	468 Malaysian pilgrims	Cross-sectional survey conducted in pilgrims recruited at a Hajj course at Universiti Sains Malaysia (USM), Kelantan,	ILI ² : 78.2%	Influenza: 37.4% Pneumococcal: 31.6%	Hashim <i>et al.</i> , 2016 (J Travel Med)	[25]

Malaysia, at Hajj Building Complex, Malaysia and in Mecca, Saudi Arabia. Study based on post-Hajj self-questionnaires collected on return						
2013	839 African pilgrims	Cross-sectional survey conducted in returning pilgrims recruited at the "Hajj village" special area at Kotoka International Airport, Ghana. Study based on face-to-face interview	Cough: 70.7% Sore throat: 40.9% Elevated temperature: 18.4% Runny nose or sneezing: 18.13% Breathing difficulty: 14.8%	Not specified	Annan <i>et al.</i> , 2015 (Trop Med Int Health)	[17]
2014	270 Indian pilgrims	Cross-sectional survey conducted in pilgrims recruited at departure from Kempegowda International Airport, Bangalore, India. Study based on telephone interview on return	ILI ² : 66.3%	Influenza: 1.1%	Fatema <i>et al.</i> , 2015 (IJPMN)	[26]

2012-2014	382 French pilgrims	Longitudinal survey conducted in pilgrims recruited at a specialized Hajj travel agency, Marseille, France. Study based on medical evaluation during travel	ILI ² : 46.2% Cough: 80.9% Sore throat: 91.0% Rhinitis: 78.7% Hoarseness: 63.0% Myalgia: 48.3% Subjective fever: 47.3%	Not specified	Gautret <i>et al.</i> , 2015 (Travel Med Infect Dis)	[16]
2007	106 Malaysian pilgrims	Longitudinal survey conducted in pilgrims enrolled in the National Pilgrim Management and Fund Board, Malaysia. Study based on follow-up during travel	Cough (average of the 6 weeks of stay): 39.5% Runny nose (average of the 6 weeks of stay): 25.5% Sore throat (average of the 6 weeks of stay): 18.5% Fever (average of the 6 weeks of stay): 7.1%	Influenza: 61.3%	Hasan <i>et al.</i> , 2015 (J Immigr Minor Health)	[51]
2013	1676 pilgrims (Paired cohort: 692 pilgrims/ Nonpaired cohort: 514 pilgrims at arrival and 470	Cross-sectional survey (unpaired cohort) and longitudinal survey (paired cohort) conducted in	ILI: 61.9%	Influenza: 21.9% Pneumococcal: 1.2%	Memish <i>et al.</i> , 2015 (Clin Microbiol Infect)	[28]

	pilgrims at Mina) from 13 countries (Africa/Asia/USA/Europe)	pilgrims recruited on arrival at Jeddah airport. Study based on post-Hajj face-to-face interview conducted at Mina				
2011 and 2012	3203 pilgrims (1590 pilgrims at the beginning of the Hajj and 1613 pilgrims at the end of the Hajj) from 18 countries in Africa or Asia	Cross-sectional survey conducted in pilgrims recruited at Mecca for the beginning-Hajj cohort and Mina for the end-Hajj cohort. Study based on face-to-face interview	URTI during Hajj (for the end-Hajj cohort): 29.2%	Influenza or pneumococcal ⁴ (beginning-Hajj cohort versus end-Hajj cohort): 45.8% versus 76.7%, respectively	Memish <i>et al.</i> , 2015 (Clin Microbiol Infect)	[27]
2011	164 Australian pilgrims	Cross-sectional survey conducted in pilgrims recruited at Mina encampment. Study based on post-Hajj face-to-face interview	ILI ³ : 63.4% Cough: 46.3% Sore throat: 34.7% Fever: 23.8% Runny nose: 23.8% Sputum: 12.8% Muscle pain: 9.7%	Not specified	Barasheed <i>et al.</i> , 2014 (Infect Disord Drug Targets)	[20]

			Headache: 8.5%			
			Shortness of breath: 2.4%			
2013	1038 pilgrims from Saudi Arabia, Australia and Qatar	Cross-sectional survey conducted in pilgrims recruited at Mina encampment. Study based on post-Hajj face-to-face interview	ILI ⁴ : 11% Sore throat: 59% Cough: 40% Runny nose: 34%	Influenza (Australian versus Qatari versus Saudi pilgrims): 87% versus 80% versus 20%, respectively	Barasheed <i>et al.</i> , 2014 (Virol Sin)	[29]
2013	129 French pilgrims	Longitudinal survey conducted in pilgrims recruited at a specialized Hajj travel agency, Marseille, France. Study based on medical evaluation during travel	ILI ² : 47.3% Cough: 86.8% Sore throat: 82.9% Rhinorrhea: 72.1% Myalgia: 50.4% Fever: 49.6% Dyspnea: 21.7%	Influenza: None in 2013 and 44.2% in 2012 Pneumococcal: 51.2%	Benkouiten <i>et al.</i> , 2014 (Emerg Infect Dis) Gautret <i>et al.</i> , 2014 (Emerg Infect Dis)	[18, 21]
2012	169 French pilgrims	Longitudinal survey conducted in pilgrims recruited at a specialized Hajj travel agency, Marseille,	ILI ² : 47.3% Cough: 83.4% Sore throat: 79.7%	Influenza: 45.6% Pneumococcal: 35.9%	Benkouiten <i>et al.</i> , 2014 (Clin Infect Dis) Benkouiten <i>et al.</i> ,	[19, 22, 23]

		France. Study based on medical evaluation during travel	Rhinorrhea: 68.5% Myalgia: 46.5% Feverishness: 45.4% Dyspnea: 19.6%		2013 (Clin Infect Dis) Gautret <i>et al.</i> , 2013 (Clin Microbiol Infect)	
2006	295 Iranian pilgrims	Longitudinal survey conducted in pilgrims recruited at a Hajj caravan. Study based on medical evaluation during travel	Runny nose: 51.7% Dry coughs: 51.7% Hoarseness: 47.7% Yellowish-greenish sputum: 42.8% Nose congestion: 38.8% Purulent Post-Nasal Discharge: 35.5% Sore Throat: 34.2% Painful swallowing: 23.8% Throat itch: 28.6% Fever: 26.8% Myalgia: 24.6% Feeling chills: 17.8%	Influenza and pneumococcal: 63.7% Influenza or pneumococcal: 26.4% Neither: 6.4% Incomplete information: 3.5%	Dabiran <i>et al.</i> , 2014 (Health)	[55]

2004-2008	254823 Iranian pilgrims (30037 pilgrims in 2004, 75676 in 2005, 48678 in 2006, 71595 in 2007, and 28837 in 2008)	Longitudinal survey conducted in pilgrims recruited at 1352 Hajj caravans. Study based on medical evaluation during travel	Common cold like illness (total): 47.1% ILI ⁵ (total): 10.7%	Influenza (2004 versus 2005): 75.2% versus 88.3%, Pneumococcal (2004 versus 2005): 2.5% versus 8.9%, respectively	Razavi <i>et al.</i> , 2014 (Med J Islam Repub Iran) Razavi <i>et al.</i> , 2013 (Med J Islam Repub Iran) Meysamie <i>et al.</i> , 2006 (Saudi Med J)	[47, 48, 46]
2010	1507 pilgrims	Longitudinal survey conducted in pilgrims recruited at primary health care centers in Riyadh, Saudi Arabia (for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return	URTI ⁶ : 53.1%	Influenza: 94.4%	Al-Jasser <i>et al.</i> , 2013 (East Mediterr Health J) Al-Jasser <i>et al.</i> , 2012 (Saudi Med J) Al-Jasser <i>et al.</i> , 2011 (Saudi Epidemiology Bulletin)	[32, 33, 36]
2009	274 French pilgrims	Longitudinal survey conducted in	ILI ² : 8.0%	Influenza: 97.4%	Gautret <i>et al.</i> , 2013	[31, 37]

		pilgrims recruited at a travel medicine clinic of a university hospital, France (for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return	Cough: 48.5% Sore throat: 36.1% Rhinorrhea: 23.7% Sputum: 13.5% Subjective fever: 10.9% Myalgia: 9.5% Shortness of breath: 2.9% Voice failure: 2.9%	Influenza A(H1N1): 5.8% Pneumococcal: 31.4%	(Travel Med Infect Dis) Gautret <i>et al.</i> , 2011 (J Travel Med)	
2006	338 Iranian Pilgrims	Longitudinal survey conducted in pilgrims recruited at a Hajj and pilgrimage organization at Chaharmahal va Bakhtiari Province, Iran. Study based on post-Hajj face-to-face interview	Cough: 70.0% Hoarseness: 53.6% Sore throat: 49.7% Coryza: 43.8% Wheezing: 43.5% Myalgia: 30.8% Dyspnea: 17.8%	Not specified	Imani <i>et al.</i> , 2013 (International Journal of Travel Medicine & Global Health)	[52]
2012	541 Australian pilgrims	Cross-sectional survey conducted in pilgrims recruited at Mina encampment. Study based on post-Hajj face-to-face interview	AFRI ⁷ : 9%	Not specified	Rashid <i>et al.</i> , 2013 (Med J Aust)	[30]

2009	186 US pilgrims	Longitudinal survey conducted in pilgrims recruited at pretravel clinic for Hajj travelers in Minnesota, US, and Arab Community Center for Economic and Social Services at multiple settings, including mosques, community health clinics, and the Detroit Wayne County International Airport, in Michigan, US. Study based on post-Hajj face-to-face and telephone interview	Cough: 30.1% Sneezing: 25.8% Sore throat: 15.6% Fever: 13.4% Congestion: 8.6% Breathing problems: 2.1% “Bronchitis” ⁸ : 1.1% ILI ⁹ : 9.7%	Influenza: 63.0% Influenza A(H1N1): 38.7%	Balaban <i>et al.</i> , 2012 (J Travel Med)	[34]
2010	1659 Afghan pilgrims	Longitudinal survey conducted in pilgrims recruited at four transit areas located next to the Kandahar, Balkh, Hirat and Kabul airports, Afghanistan. Study based on post-Hajj telephone interview	ILI ² : 37.8%	Not specified	Saeed <i>et al.</i> , 2012 (J Epidemiol Glob Health)	[35]

2009	305 Iranian pilgrims	Cross-sectional survey conducted in returning pilgrims recruited Shiraz Airport, Iran	Fever: 11.1% Cough: 48.2% Sore throat: 46.2% Nasal symptoms: 60.6% Myalgia: 31.8%	Influenza: 97.7%	Ziyaeyan <i>et al.</i> , 2012 (Influenza Other Respir Viruses)	[53]
2010	1717 pilgrims	Cross-sectional survey conducted in returning pilgrims recruited at King Abdulaziz International Airport, Jeddah	Cough: 72.2%	Influenza: 52.4%	Maslamani <i>et al.</i> , 2011 (Saudi Epidemiology Bulletin)	[54]
2007	387 Malaysian pilgrims	Cross-sectional survey conducted in returning pilgrims recruited at transit centers at Jeddah and Medina	ILI ² : 40.1 Cough: 91.5% Runny nose: 79.3% Fever: 59.2% Sore throat: 57.1%	Influenza: 72.9%	Deris <i>et al.</i> , 2010 (J Travel Med) Deris <i>et al.</i> , 2010 (Trop Biomed)	[14, 15]
2007	394 Malaysian pilgrims	Cross-sectional survey conducted in returning pilgrims recruited at transit centers at Jeddah and Medina	Cough: 90.1% Runny nose: 78.2% Fever: 58.4% Sore throat: 56.3%	Not specified	Deris <i>et al.</i> , 2009 (Saudi Med J)	[73]
2006	580 French pilgrims	Longitudinal survey conducted in	Cough: 60.6%	Influenza: 34.3%	Gautret <i>et al.</i> , 2009	[49]

		pilgrims recruited at a travel medicine clinic of a university hospital, France (for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return	Fever: 16.6%		(Clin Microbiol Infect)	
2004	170 Iranian pilgrims	Longitudinal survey conducted in pilgrims recruited to departure from Iran (details not provided). Study based on medical follow-up at Mina encampment	Common cold ¹⁰ : 57.0% ILI ¹¹ : 10.9%	Not specified	Razavi <i>et al.</i> , 2007 (IJCID)	[38]
2002	1027 domestic pilgrims	Longitudinal survey conducted in pilgrims recruited at primary health care centers in Riyadh, Saudi Arabia (for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return	ARI ¹² : 39.8%	Not specified	Choudhry <i>et al.</i> , 2006 (East Mediterr Health J)	[39]

2004	995 pilgrims from Riyadh	Longitudinal survey conducted in pilgrims recruited from randomly selected Hajj groups in Riyadh, Saudi Arabia. Study based on post-Hajj telephone interview	ARI ¹³ : 25.6%	Not specified	Abdin <i>et al.</i> , 2005 (Saudi Epidemiology Bulletin)	[40]
2003-2004	51100 Iranian pilgrims (32370 pilgrims in 2003 and 18730 pilgrims in 2004)	Longitudinal survey conducted in pilgrims recruited at 180 Hajj caravans in 2003 / 110 caravans in 2004. Study based on medical evaluation during travel	ILI ¹⁴ in 2003: 70.1% ILI ¹⁴ in 2004: 35.8%	Influenza (2003 versus 2004): 10.7% versus 75.2%, respectively	Razavi <i>et al.</i> , 2005 (Acta Medica Iranica) Razavi <i>et al.</i> , 2004 (Acta Medica Iranica)	[41, 42]
2003	115 UK pilgrims	Longitudinal survey conducted in pilgrims recruited at East London Mosque, London, UK. Study based on medical evaluation after travel	Respiratory symptoms: 80.9%	Influenza: 26.1%	El Bashir <i>et al.</i> , 2004 (Emerg Infect Dis)	[56]
2003	1027 pilgrims from Riyadh	Longitudinal survey conducted in pilgrims recruited at 10 randomly selected primary health care centers in Riyadh, Saudi Arabia	ARI ¹⁵ : 39.8%	Influenza: 10.5%	Al-Mudameigh <i>et al.</i> , 2003 (Saudi Epidemiology Bulletin)	[43]

		(for the mandatory pre-Hajj meningococcal vaccination). Study based on telephone interview on return				
1999	412 domestic and international pilgrims	Cross-sectional survey conducted in pilgrims recruited at Mina. Study based on post-Hajj self- administered questionnaires	Runny nose: 18.0% Cough: 14.0% Sore-throat: 12.0%	Not specified	Fatani <i>et al.</i> , 2001 (Saudi Epidemiology Bulletin)	[13]
1999	2070 Pakistani pilgrims	Longitudinal survey conducted in pilgrims recruited in organized groups in Pakistan. Study based on medical evaluation during travel	ILI ¹⁶ : 47.9% Documented fever $\geq 38.8^{\circ}\text{C}$: 29.8% URTI ¹⁷ : 72.2%	Influenza: 54%	Qureshi <i>et al.</i> , 2000 (Vaccine)	[44]

¹ILI was defined according to the presence measured fever of $\geq 38^{\circ}\text{C}$, and cough; with onset within the last 10 days.

²Influenza-like illness (ILI) was defined according to the presence of the triad of cough, subjective fever and sore throat.

³ILI was defined as subjective (or proven) fever plus one respiratory symptom (e.g. dry or productive cough, runny nose, sore throat, shortness of breath).

⁴ILI was defined as subjective (or proven) fever and at least one respiratory symptom such as cough, sore throat and rhinorrhea.

⁵ILI was defined as symptoms and signs such as: sudden headache, dry cough, high grade fever, myalgia, coryza, malaise and loss of appetite with an abnormal general appearance.

⁶Upper respiratory tract infections (URTI) was defined as any person who reported having developed at least one of the constitutional symptoms (fever, headache, myalgia) and one of the local symptoms (running nose, sneezing, throat pain, cough with /or without sputum) after reaching Mecca for the Hajj or within 2 weeks from return to Riyadh.

⁷Acute febrile respiratory infection (AFRI) was defined as the presence of subjective fever plus at least one respiratory symptom (cough, sore throat, runny nose or breathlessness).

⁸Two travelers who reported “bronchitis” as a symptom were also included.

⁹ILI was defined as fever plus sore throat and/or coughing.

¹⁰Common cold was defined as sore throat with coryzal symptoms, and low grade fever.

¹¹ILI was defined as fever $>38.5^{\circ}\text{C}$, myalgia, low back pain, coryzal symptoms and cough.

¹²Acute respiratory infection (ARI) was defined as one of the constitutional symptoms (fever, headache, myalgia) along with one of the local symptoms (running nose, sneezing, throat pain, cough with/without sputum, difficulty breathing).

¹³ARI was defined as any person suffering from at least one of the constitutional symptoms (fever, headache, myalgia) along with one of the local symptoms (runny nose, sneezing, throat pain, cough with/without Sputum, difficulty in breathing) developing after reaching Makkah for the Hajj.

¹⁴ILI was defined as cough and fever $>38^{\circ}\text{C}$ with or without the coryzal symptoms and myalgia.

¹⁵ARI was defined as any person suffering from at least one of the constitutional symptoms (fever, headache, myalgia) along with one of the local symptoms (runny nose, sneezing, throat pain, cough with/without Sputum, difficulty in breathing) developing after reaching Mecca for the Hajj.

¹⁶ILI was defined as sore throat with either temperature $\geq 38.8^{\circ}\text{C}$ or cough.

¹⁷Cough or sore throat or rhinorrhea or muscle ache or headache.

Table 2. Studies conducted among ill Hajj pilgrims at health care facilities

Hajj season	Study population	Recrutement	Proportion of ill patients with respiratory symptoms globally (%)	Proportion of ill patients with pneumonia (%)	Study	Ref.
2012-2014	185 Turkish patients (87.5% were pilgrims) returning to Turkey from the Arabian Peninsula countries	15 referral Turkish centers with infectious diseases departments (inpatients)	URTI ¹ : 33.1% Acute tracheobronchitis ² : 13.6% Acute exacerbation of COPD ³ : 8.9%	50.3%	Erdem <i>et al.</i> , 2016 (Eur J Clin Microbiol Infect Dis)	[64]
2008	4136 patients (94.9% were pilgrims) from 82 nationalities	13 randomly selected Mina primary health care centers (outpatients)	Common cold: 20.6% Pharyngitis: 23.7% Bronchitis: 9.6% Tonsillitis: 4.2%	0.2%	Alzahrani <i>et al.</i> , 2012 (J Infect Public Health) Alzahrani <i>et al.</i> , 2009 (Saudi Epidemiology Bulletin)	[59, 60]
2009-2010	452 pilgrims from over 40 nationalities	Intensive care unit of 15 hospitals in Mecca, Mina, Arafat, and Medina (inpatients)	Not specified	27.2%	Mandourah <i>et al.</i> , 2012 (BMC Infect Dis)	[65]
2009	3087 Saudi and non-Saudi	Ear, nose, and throat clinic at Al-	Pharyngitis: 45.7%	Not specified	Alherabi <i>et al.</i> ,	[58]

	patients (47.5% were pilgrims)	Noor Specialist Hospital, Mecca (mostly outpatients)	URTI ⁴ : 42.1%		2011 (Saudi Med J)	
2008	1047 Saudi and non-Saudi patients (34.5% were pilgrims)	Ear, nose, and throat clinic at Al-Noor Specialist Hospital, Mecca (mostly outpatients)	Pharyngitis: 61.0% URTI ⁴ : 18.6% Tonsillitis: 5.5% Otitis media: 2.2%	Not specified	Alherabi <i>et al.</i> , 2009 (Saudi Med J)	[61]
2004	165 pilgrims	Two intensive care units (King Faisal Hospital and King Abdul Aziz Hospital) in Mecca (inpatients with sepsis)	Not specified	54.8%	Baharoon <i>et al.</i> , 2009 (Travel Med Infect Dis)	[66]
2007	2411 patients	Emergency room of Al-Anssar Hospital and 4 primary health care centers in Medina (in and outpatients)	Not specified	1%	Al-Quwaidhi <i>et al.</i> , 2008 (Saudi Epidemiology Bulletin)	[67]
2007	248 pilgrims	Two randomly selected Mina hospitals (Mina al Tawarri & Mina El-Jesser) (outpatients)	Cough: 28.2% Dyspnea: 27.4% Fever: 25.0% Running nose: 16.5% Chest pain: 15.3%	Not specified	Khamis <i>et al.</i> , 2008 (J Egypt Public Health Assoc)	[72]

2004	140 patients (97.9% were pilgrims)	Intensive care units in Mina and Arafat hospitals (inpatients)	Respiratory failure: 5.0% Upper airway obstruction: 0.7%	22.1%	Madani <i>et al.</i> , 2007 (Ann Saudi Med)	[68]
2005	689 pilgrims from 49 countries	Tertiary care hospital in Mina (inpatient medical departments)	Dyspnea: 38.3% Chest pain: 24.8% Cough: 22.1% Fever: 19.2%	26.0%	Khan <i>et al.</i> , 2006 (Saudi Med J)	[69]
2003	575 patients (97.4% were pilgrims)	Seven hospitals in Mina and Arafat (inpatient medical wards)	URTI ⁴ : 4.7% Acute bronchitis: 1.7%	29.4%	Madani <i>et al.</i> , 2006 (Ann Saudi Med)	[62]
2002	160 patients	Two hospitals in Arafat and two hospitals in Mina (in patient medical wards)	URTI ⁴ : 3.1% Dyspnea: 53.0% Cough: 49.0% Fever: 47.0% Chest pain: 12.5%	39.4%	Al-Ghamdi <i>et al.</i> , 2003 (Saudi Med J)	[70]
1993	7676 pilgrims	Emergency Department of Al-Noor Hospital in Mecca (in and outpatients)	Sore-throat: 6.8% Common cold: 6.0% URTI ⁴ : 4.4% Bronchitis: 3.7%	2.0%	Al-Harbi <i>et al.</i> , 2000 (J Family Community Med)	[63]

			Headache: 1.6%			
			Cough: 1.2%			
1993	773 pilgrims	King Abdul Aziz hospital in Medina (inpatient medical wards)	URTI ⁴ : 7.1%	45.8%	Yousuf <i>et al.</i> , 1995 (Ann Saudi Med)	[71]
1992	141 Pakistani pilgrims	King Abdul Aziz hospital in Medina (inpatient medical wards)	URTI ⁴ : 1.4% Acute bronchitis: 1.4%	29.1%	Yousuf <i>et al.</i> , 1993 (PJMR)	[57]

¹Upper respiratory tract infection (URTI) was defined as an acute infection that includes tonsillitis, pharyngitis, laryngitis, sinusitis, otitis media, and the common cold.

²Acute tracheobronchitis was defined as a patient with dry cough and/or low-grade of fever (< 38 °C), sub-sternal pain, and fatigue in the absence of opacities on chest X-ray.

³Acute exacerbation of chronic obstructive pulmonary disease (COPD) was defined as an association with increased frequency and severity of coughing and/or shortness of breath and wheezing, increased amount of sputum production, and/or a change in appearance of sputum in a patient with COPD.

⁴Was not defined.

Table 3. Prevalence of cough, influenza-like illness, upper respiratory tract infection and pneumonia reported in the included studies

Symptoms	Prevalence (%)	Range (%)
Cough (in cohorts of Hajj pilgrims)	1.9	1.9-91.5
	14.0	
	30.1	
	39.5	
	40.0	
	46.3	
	48.2	
	48.5	
	51.7	
	60.6	
	63.0	
	70.0	
	70.7	
	72.2	
	80.9	
	83.4	
	86.8	
	90.1	
	91.5	
Cough (in ill Hajj pilgrims at health care facilities)	1.2	1.2-49
	22.1	
	28.2	
	49.0	
ILI ¹ (in cohorts of Hajj pilgrims)	8.0	8.0-78.2
	9.7	
	11.0	

	10.7	
	10.9	
	30.4	
	35.8	
	37.8	
	40.1	
	46.2	
	47.3	
	47.3	
	47.9	
	61.9	
	63.4	
	66.3	
	70.1	
	78.2	
URTI ² (in cohorts of Hajj pilgrims)	29.2	29.2-72.2
	53.1	
	72.2	
URTI ² (in ill Hajj pilgrims at health care facilities)	1.4	1.4-42.1
	4.4	
	4.7	
	7.1	
	18.6	
	33.1	
	42.1	
Pneumonia (in ill Hajj pilgrims at health care facilities)	0.2	0.2-54.8
	1.0	
	2.0	
	22.1	
	26.0	

27.2

29.1

29.4

39.4

45.8

50.3

54.8

¹Influenza-like illness²Upper respiratory tract infection

Figure 1. Flow diagram